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The Assessment of Quality of Life, Depression and Anxiety in Siblings of Children with Cancer: A Case-Control Study

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OBJECTIVE

Pediatric cancers may have traumatic, adverse effects on healthy siblings of children with cancer. The majority of studies on the subject have been performed in Western societies, and few controlled studies implementing validated surveys have been performed. The aim of this study is to investigate the quality of life, prevalence of anxiety and depression and associated factors in healthy siblings of children with cancer.

METHODS

Sixty children aged 8-16 years-old with siblings with cancer were included as the case group and sixty children with siblings without cancer were enrolled as the control group. The Revised Child Anxiety and Depression Scale (RCAD-S) and the Questionnaire for Quality of Life Assessment for Children and Adolescents Parent Form (Kid-KINDL) were used to evaluate anxiety/depression symptoms and quality of life respectively.

RESULTS

The case group consisted of 30 boys and 30 girls (12.08 ± 2.61 years), and the control group of 31 boys and 29 girls (11.40 ± 2.11 years). Depression/anxiety symptoms were significantly higher in the case group than in the control group (p<0.05). Quality of life total score was significantly lower in the case group than in the control group (p<0.05). Being siblings of same gender was determined to be associated with impaired quality of life (B=8.81 CI: 1.56-49.65, p=0.014) and presence of depression/anxiety (B=6.89 CI: 1.29-36.72, p=0.024).

CONCLUSION

Professionals should include healthy siblings of children with cancer when assessing the psychosocial effect of pediatric cancer, and should adopt a multidimensional approach in caring for healthy siblings of children with cancer.

Keywords: Anxiety; depression; pediatric cancer; siblings; quality of life. Copyright © 2021, Turkish Society for Radiation Oncology

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Introduction

Pediatric cancer is one of the main causes of childhood mortality and a public health threat of growing importance.[1] Approximately 250.000 children aged 0-19 are diagnosed with cancer and 100.000 children die because of the disease worldwide every year.[2,3]

Despite cancer is a physical disease, it has significant mental and psychosocial impacts. When a family member is diagnosed with cancer, this may also affect all other members.[4,5] In families with multiple children, pediatric cancer may be especially challenging for healthy siblings.[4] Numerous changes occur in the daily lives of healthy siblings of children with cancer (HSCC), including alterations in day-to-day routines, family roles, and emotional/behavioral and educational problems rise.[6,7] The daily routines of HSCC are interrupted due to hospital visits and admissions of the child diagnosed with cancer.[6,8] Roles within the family are altered together with changes in the family system. Individual responsibilities increase, and the caregiver's assistance to the HSCC decrease as a result. [6,9] HSCC experience more emotional problems than the unaffected people such as fear, anxiety, shock, loneliness, sadness, anger, guilt, and helplessness.[10-12]

Despite the growing interest in recent years, there has been little agreement on the psychosocial impacts (such as depression/anxiety and quality of life) and associated risk factors of pediatric cancer on healthy siblings. [4,13,14] It can be seen that the studies conducted on HSCC have suffered several methodological limitations. In a recent review on the effects of pediatric cancers on healthy siblings, the majority of studies were reported to involve low numbers of participants and no control groups whatsoever. [4] In the controlled few studies, there were non-matched control groups due to using Cancer Survivor Study data in which most subjects in control groups were either cancer survivors or had cancer. Additionally, there has been a few studies implementing validated surveys. [4]

Cultural norms have been considered important factors affecting the psychosocial outcomes of cancer on the family system.[15] However, most of the studies on psychosocial effects of cancer come from the Western countries with only few studies from non-Western populations.[5] In a current review study (2020), the researchers found no articles on the psychosocial status of siblings of children with cancer in Turkey.[16] This condition leaves a gap in the literature. In the current study, the authors seek to obtain data which will help to address these gaps.

Psychosocial effects of pediatric cancer on HSCC have several different dimensions while depression/anxiety and quality of life have been frequently investigated issues with inconsistent findings across studies. [4,6,17] The purpose of this study was to investigate the psychosocial effects of pediatric cancer on HSCC in a non-Western population with particular attention to the depression/anxiety and quality of life, and associated factors.

This research considered the following questions:

- I. Are depression/anxiety symptoms more common in HSCC than in the unaffected population?
- II. Is there any difference in quality of life scores between case and control groups?
- III. What is the relation between quality of life and depression/anxiety symptoms in HSCC?
- IV. What are the factors associated with impairment of quality of life and presence of depression/anxiety?

Materials and Methods

Participants

This study was performed at the Gaziantep University Medical Faculty, Turkey, between August 2018 and January 2019. The study consisted of case and control groups.

Inclusion criteria were a) age 8-16 years, b) no diagnosis of cancer in either of the parents, c) absence of any chronic medical or neurological disease in the child and d) the parent being literate and possessing sufficient Turkish language skills to complete the study form. Further conditions were a diagnosis of cancer in a sibling for at least three months prior in the case group, and absence of any current or previous history of cancer in any sibling for the control group. No exclusion criteria were imposed concerning type or stage of pediatric cancers. Parents unwilling to participate and families with a parent suffering from psychotic disorder or intellectual disability were excluded from the study.

Parents of children with cancer were approached during their clinical visits to pediatric hematology and oncology clinics. Parents were provided information about the study and healthy children of parents who gave informed consent were enrolled in the case group. If the children with cancer have more than one sibling, only the nearest-age sibling was included in the study. Control group consisted of children presenting to the pediatric clinic due to upper respiratory tract infection (URTI) or for routine health checks. They were required to have similar sociodemographic character-

istics to those of the case group and no diagnosis of cancer in the family.

Of those parents (n=185) who were eligible for the participation, 64.9 percent (n=120) were enrolled in the study. Of those parents who did not give consent for the participation (n=65) main reasons for refusing were; not having enough time (n=43; 66.1 %), feeling anxious or distressed (n=16; 24.6%) and the concern of parents about it would not be useful (n=6; 9.2 %).

Parents completed a Personal Information Form, the Revised Children's Anxiety and Depression Scale (RCADS), and the Questionnaire for Quality of Life Assessment for Children and Adolescents Parent Form (Kid-KINDL). The scales were completed for the HSCC in the case group and for the child presenting for routine health checks in the control group. In accordance with the Declaration of Helsinki, approval for the study was obtained from the Gaziantep University Ethics Committee on 01.08.2018 (No: 2018/180).

Measures

Personal Information Form

Parents agreeing to take part in the study completed a personal information form prepared by the authors. This form consisted of questions inquiring into sociodemographic characteristics such as children's age and gender, parental education levels (years), and family income status (below or above minimum wage as declared by Turkish government).[18] For the family income status we defined the groups as low income (below minimum wage) or normal income (above minimum wage). The personal information form also contained questions about the age and gender of the child with cancer, the diagnosis, and the duration of disease (months).

Revised Child Anxiety and Depression Scale (RCAD-S)

The RCAD-S was developed by Chorpita et al.[19] The validity and reliability of the Turkish language version were established by Görmez et al.[20] The Cronbach alpha coefficiency of the Turkish-language form of the scale was calculated as 0.95. The Cronbach α coefficiency of the RCAD-S in the present study was 0.88. The scale consists of 47 items. These are answered by parents based on a four-point Likert (0=never, 1=sometimes, 2=frequently, and 3=never). The scale screens for depression, and anxiety disorders (separation anxiety disorder, panic disorder, generalized anxiety disorder, and social phobia). The scale elicits Total

Anxiety and Total Depression/Anxiety scores derived from the total of the items concerning these disorders. It provides categorical and dimensional data concerning these disorders. The cut-off point for total depression/anxiety score was 33 or above. Subjects with total depression/anxiety scores of 33 or more were regarded as having depression/anxiety.[20]

Questionnaire for Quality of Life Assessment for Children and Adolescents Parent Form (Kid-KINDL)

Kid-KINDL was developed by Ravens-Sieberer et al. to assess health-related quality of life.[21] The validity and reliability of the Turkish language version were studied by Eser et al.[22] The Cronbach alpha coefficiency of the Turkish-language form of the scale was calculated as 0.78. The Cronbach α coefficiency of the RCAD-S in the present study was 0.74. It consists of five categories based on a five-point Likert scale (1: Never, 2: Rarely, 3: Sometimes, 4: Frequently, 5: Always). The scale consists of 24 items in six dimensions, physical wellbeing, emotional well-being, self-esteem, family, social relations, and school. Mean Average scores for each subgroup are calculated and converted into a value between 0 and 100. Scorings are positively oriented, with high scores indicating good quality of life. A general quality of life score was used for statistical analysis in which a quality of life score for each domain and all domains together were calculated. A cut-off point of 70 was adopted for the general quality of life score. Total quality of life scores below 70 were regarded as a sign of impaired quality of life.[23,24]

Treatment Intensity

The Intensity of Treatment Rating Scale 3.0 (ITR-3) was used to determine the intensity of pediatric cancer treatment. The content validity (r=0.88) and interrater reliability (r=0.86) of ITR-3 were established by Kazak et al. ITR-3 has four levels of treatment intensity (1=least intenseive, 2=moderately intensive, 3=very intensive, and 4=most intensive).[25]

Data Analysis

Statistical analysis was performed on SPSS Windows 21.0 software. Percentage, arithmetic average, and standard deviation were employed. Distribution of data was assessed using the Kolmogorov Smirnov test. Student's t-test, with Pearson correlation analysis for correlation, was applied for normally distributed data, while the Mann-Whitney U test was used for non-

normally distributed data. Relations between qualitative variables were examined using the chi-square test. p<0.05 was regarded as statistically significant. Factors related to presence of depression/anxiety and impaired quality of life were evaluated by composing models using binary logistic regression analyses. Since there have been no similar studies using the Turkish version of the Revised Child Anxiety and Depression Scale in the literature, power analysis could not calculate. Post-hoc power analysis of 120 participants showed a power of 79.2% in total depression/anxiety scores using an independent t-test with a 0.05 two-sided significance level.

Results

One hundred twenty subjects aged 8-16 years old were included in the study. The study sample consisted of case (12.08±2.61 years old) and control (11.40±2.11 years old) groups with each group including 60 sub-

^aIndependent sample t-test. ^bχ² test, ^cMann–Whitney U-test

jects. The two groups were statistically similar in terms of the age, gender, income level, and parental education levels (p>0.05 for all). Table 1 shows the descriptive characteristics of the study subjects.

The total RCAD-S score in our case group was significantly higher than the control group (Independent Sample t-test, t-score=2.742, p=0.007). RCAD-S subscale analysis revealed significantly higher panic disorder, social phobia, and depression scores in the case group (p<0.05 in all measures). Case and control group RCAD-S scores are summarized in Table 2.

In addition to anxiety and depression scores, total quality of life scale score was also significantly lower in the case group compared to the control group (Independent Sample t-test, t-score=-3.040, p=0.003). Quality of life scores in the school (Mann–Whitney U-test, z-score=-2.932, p=0.003) and self-esteem (Independent Sample t-test, t-score=-4.027, p<0.001) domains were significantly lower compared to those in the con-

Variable	Case group (n=60)	Control group (n=60)	р
Age (years)	12.08±2.61	11.40±2.11	0.120a
Gender, n (%)			1.000 ^b
Female	30 (50.0)	29 (48.3)	
Male	30 (50.0)	31 (51.7)	
Average duration of parental education (years)	6.20±2.82	7.49±4.30	0.132°
Family income status, n (%)			0.307 ^b
Minimum wage or less	41 (68.3)	46 (76.7)	
Above the minimum wage	19 (31.7)	14 (23.3)	
Respondent parent, n (%)			
Female	49 (81.7)	44 (73.3)	274 ^b
Age	34.53±5.08	33.60±5.58	340°
Time since diagnosis, n (%)			
>1 year	25 (41.7)	-	
≤1 year	35 (58.3)	-	
Type of pediatric cancer, n (%)			
ALL	36 (60)	-	
AML	12 (20)	-	
Others	12 (20)	-	
Children with cancer, n (%)			
Female	23 (38.3)	-	
Male	37 (61.7)	-	
Age of children with cancer, n (%)			
Treatment Intensity		-	
Least intense	3 (5.4)	-	
Moderately intensive	31 (54.4)	-	
Very intensive	12 (21.4)	-	
Most intensive	10 (17.9)	-	

Table 2 Revised Child Anxiety and Depression Scale scores of case and control groups

	Case group (n=60)#	Control group (n=60)#	р
RCAD-SAD	4.63±3.43	3.80±2.46	0.132ª
RCAD-GAD	3.87±2.81	3.61±2.77	0.591 ^b
RCAD-PD	3.60±2.98	2.00±1.42	0.011 ^b
RCAD-SoP	7.06±5.04	5.36±3.17	0.031a
RCAD-OCD	4.36±3.36	3.20±3.01	0.051a
RCAD-Ta	23.46±14.31	18.23±11.39	0.030a
RCAD-MDD	6.15±5.00	3.25±2.76	<0.001a
RCAD-Ts	29.62±18.39	21.46±13.44	0.007ª

^aIndependent sample t-test. ^bMann–Whitney U-test. ^aData presented as mean±SD. Bold data, p<0.05 (significance). MDD: Major Depressive Disorder; GAD: Generalized Anxiety Disorder; SAD: Separation Anxiety Disorder; PD: Panic Disorder; SoP: Social Phobia; OCD: Obsessive–Compulsive Disorder; RCAD-Ta: RCAD Total Anxiety Scores; RCAD-Ts: Total RCAD-S Scores

trol group. Case and control group quality of life scores are summarized in Table 3.

High Kid-KINDL scores indicate high quality of life, while high RCAD-S scores indicate a high frequency of psychiatric symptoms. Correlation analysis revealed significant negative correlation between total RCAD-S scores and Kid-KIND-T scores (p<0.001, correlation coefficient=-0.545). Figure 1 shows a correlation scatter plot of total RCAD-S and Kid-KIND-T scores in case group.

A binary regression model was established for the independent determination of predictors of presence of depression/anxiety and impairment of quality of life in HSCC. In producing that model, total depres-

Table 3 Questionnaire for Quality of Life Assessment for Children and Adolescents Parent Form scores of case and control groups

	Case group (n=60)#	Control group (n=60)#	р
Kid-KINDL-PW	75.42±17.78	76.14±12.20	0.796ª
Kid-KINDL-EW	74.15±16.75	78.33±19.97	0.142a
Kid-KINDL-SE	61.75±23.87	77.08±17.01	<0.001a
Kid-KINDL-Fa	75.95±16.97	79.27±23.59	0.052 ^b
Kid-KINDL-Fr	63.13±19.61	67.60±18.85	0.080 ^b
Kid-KINDL-Sc	53.60±18.61	64.27±15.26	0.003 ^b
Kid-KINDL-T	67.33±13.05	73.78±9.82	0.003ª

Notes: *Independent t-test. *Mann–Whitney U-test. *Data presented as mean±SD. Bold data, p<0.05 (significance). PW: Physical well-being; EW: Emotional well-being; SE: Self-esteem; Fa: Family; Fr: Friends; Sc: School functioning; Kid-KINDL-T: Total Kid-KINDL scores

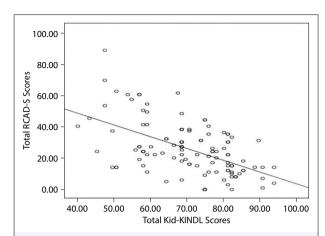


Fig. 1. The correlation scatter plot for total Revised Child Anxiety and Depression Scale (RCAD-S) scores and total Questionnaire for Quality of Life Assessment for Children and Adolescent Parent Form (Kid-KINDL) scores in the case group.

sion/anxiety scores (Total RCAD-S Scores) and total quality of life scores (Total Kid-KINDL Scores) cut-off points were used as dependent variables.[20,23,24] The independent variables used in the study were the gender of the healthy child (male→female), the child with cancer and the healthy sibling being of the same gender (absence-presence), the age of the healthy child (years), the age difference between the siblings (years), treatment intensity (1 (least intenseive) → 4 (most intensive)), recurrence (absence-presence), and low income status (high/normal income status→low income status). Significant relation was found between total depression/anxiety and the siblings being of the same gender (B=6.89 confidence interval (CI): 1.29; 36.72, p=0.024) and also the intensity of treatment (B=3.55 CI: 1.12; 11.22, p=0.031). Predictive factors for impairment of quality of life included age difference (B=1.34 CI: 1.08; 1.66, p=0.008) and the siblings being of the same gender (B= 8.81 CI: 1.56; 49.65, p=0.014). Binary logistic regression analysis concerning predictors affecting anxiety, depression and quality of life is summarized in Table 4.

Discussion

The study investigated the relationships between pediatric cancer and depression, anxiety, and quality of life in HCSS. We examined independent variables potentially associated with depression, anxiety and quality of life and found several important findings with clinical and research implications.

Table 4 Binary logistic regression analysis for predictors of impairment in quality of life and presence of depression/anxiety

	Depression/anxiety (Total RCAD-S)			Impairment in Quality of Life (Total Kid-KINDL)		
	OR	95% CI	р	OR	95% CI	р
Same gender	6.89	1.29-36.72	0.024	8.81	1.56-49.65	0.014
Female gender	0.48	0.09-2.40	0.377	0.66	0.15-2.80	0.576
Intensity of treatment	3.55	1.12-11.22	0.031	0.89	0.34-2.32	0.814
Age difference between siblings	1.16	0.96-1.40	0.114	1.34	1.08-1.66	0.008
Presence of recurrence	0.09	0.007-1.37	0.084	1.25	0.10-15.43	0.861
Age of children with cancer	0.80	0.57-1.12	0.203	0.81	0.60-1.10	0.191
Low income status	4.71	0.92-24.12	0.063	0.91	0.21-3.86	0.903

Notes: The Nagelkerke R square for total RCSD-S scores is 0.377 (p=0.015). The Nagelkerke R square for impaired quality of life is 0.310 (p=0.043). Bold data, p=0.05 (significance). Cl: Confidence Interval; OR: Odds ratio

We have found higher rates of depression and anxiety symptoms among HSCC compared to control group, the case group showing more significant depressive symptoms. We further looked for the subtypes of anxiety symptoms and found that symptoms of social anxiety and panic disorders were significantly more in HSCC. A literature review revealed that although HSCC experience negative emotions like fear, anger, loneliness, shock, jealousy, helplessness, guilt, sadness, and social withdrawal, there is little clinical agreement among the results of studies concerning the prevalence of depression and anxiety symptoms in HSCC.[4,6,12,26] Houtzager et al. (2004) reported significantly higher depression, anxiety, and social withdrawal symptoms among HSCC aged 12-18 years compared to a reference group. [17] Similarly, Alderfer et al. reported significantly higher anxiousness/depression, withdrawal/depression, related, somatic complaints and aggressive behavior in the subscales of Child Behavior Checklist (CBCL) in HSCC compared to the normal population.[27] However, several studies have reported that depression and anxiety symptoms are within normative ranges in HSCC. [13,28-30] A recent review reported that the prevalence of depression and anxiety in HSCC was clinically within normal ranges and similar to that in the groups it was compared.[4] However, it may be important to note that majority of the studies conducted on this topic come from Western countries while current study was conducted in a non-Western population with different sociocultural and family characteristics yielding different findings.[15,31] Additionally, these results are likely to be associated with using a well-matched control group in our study, unlike other studies.[4]

Other notable findings of the current study were that depression/anxiety scores were associated with the

same gender between ill and healthy siblings and treatment intensity for the sibling with cancer. Considering that the family is a system, the gender of the healthy child and the gender of the individual with cancer must be evaluated together in assessing the psychosocial effects on the healthy child. When one family member is diagnosed with cancer, healthy child in the family may be in different roles (such as sibling, offspring or grandchild).[4,5] These different roles should be considered when evaluating the effects of gender on psychosocial aspects of cancer. For example, several studies investigating the effects of parental cancer on healthy offspring have reported that girls are more at risk in terms of psychological health. Since most of these studies have involved parents with breast cancer, the affected parent and offspring have generally been female.[5] Findings from these studies raise the question of whether the psychological effects on healthy children are associated with the female gender or with the ill family member and healthy children being the same gender. Mixed findings were reported for the effect of gender on HSCC in pediatric cancer studies.[4,32,33] In our study, this was found to be associated with the siblings (healthy and patient with cancer) being of the same gender, rather than with female gender. To the best of the author's knowledge, there have been no previous studies considering the gender of the healthy child together with that of the individual with cancer. Further multi-dimensional studies of the effects of gender are needed for a better understanding of this issue. In the quantitative study of 30 HSCCs, Long et al. reported a relation between distress in the HSCC and treatment intensity.[28] In line with this report we found an association between depression/anxiety in HSCC and the intensity of treatment in sibling with cancer. Therefore, clinicians treating children with cancer should give particular attention for the healthy siblings if they are the same gender and there is intensive treatment in children with cancer.

The quality of life total score in the case group (HSCC) was significantly lower than that of the control group in the present study. This was particularly evident in the school and self-esteem domains. In a systematic review study, Alderfer et al. determined poorer quality of life in HSCC.[27] In addition, several other studies have also determined impairment of quality of life in HSCC.[17,34-36] However, a review by Long et al. reported that findings concerning quality of life of HSCC were inconsistent across studies.[4] In our study, impairment of quality of life was found to be associated with an increased age difference between healthy and ill siblings. This result may be related to unmet needs and increased responsibilities. Unmet needs are increased in younger HSCCs as well as responsibilities are increased in older HSCCs.[37,38] Both conditions may be associated with increased age difference and impairment in quality of life. This finding supports a previous study, investigating the factors predicting psychological distress and unmet needs in 106 adolescents and young adults that reporting a greater age difference between siblings among demographic variables was particularly associated with unmet needs.[37] Confirmation of this finding by our study in a different socio-cultural population may prompt clinicians to be more cautious about quality of life issues in HSCC when treating children with cancer.

Another finding in the present study was a significant negative correlation between Total-RCADS and Total-KidKINDL scores. The present finding is in agreement with a previous study reporting that family adjustment was positively correlated with anxiety and negatively correlated with quality of life.[39] To date very few studies have investigated the relation between depression /anxiety symptoms and quality of life in HSCC.[39] Despite we found a negative correlation between depression/anxiety and quality of life total scores, due to the cross-sectional design of our study, it may not show a casual relationship between these variables as bidirectional relation is quite possible.

Limitations

There are a number of limitations of this study, including its cross-sectional design, relatively small sample size, potential selection bias, and parental reports of depression/anxiety and quality of life. Further studies

with prospective design and larger samples in different cultures with parental and self-reports are needed on this topic.

Conclusion

Health professionals treating or working with children with cancer should keep in mind that cancer itself and treatment procedures may have negative psychological impact and impairment in quality of life among healthy siblings. Same gender and increased age difference between the ill and healthy siblings, and treatment intensity are among the important variables associated with depression/anxiety and impairment of quality life.

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